



Atty. Docket No.: 8654/2222

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Wilson, et al.
Serial No.: 10/790,943
Filed: March 2, 2004
Entitled: Anti-Cancer Combinations

Examiner: Delacroix Muirhei, C.
Group Art Unit: 1614
Conf. No.: 2176

CERTIFICATE OF MAILING UNDER 37 CFR 1.10

I hereby certify that the paper (and any paper or fee referred to as being enclosed) is being deposited with the United States Postal Service using Express Mail to Addressee Service, under 37 C.F.R. Section 1.10, **Express Mail Label No. EV239984235US** on this date, **May 10, 2005**, postage prepaid, in an envelope addressed to Mail Stop: Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Nancy Arsenault

Name of Person Mailing Paper

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**Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450**

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §§§ 1.56, 1.97 AND 1.98**

Dear Sir:

In accordance with the duty of disclosure under 37 CFR § 1.56, Applicant submits this Supplemental Information Disclosure Statement pursuant to 37 CFR §§ 1.97 and 1.98 in the above-identified application for consideration by the Patent Office.

A listing of the cited documents is also enclosed, as well as, for the Examiner's convenience, copies of the documents in the list.

Applicant does not intend to represent that any of the documents submitted herein are material prior art to this invention or that the list represents an exhaustive search of documents related to this invention.

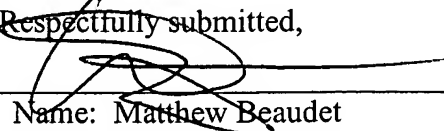
Applicant respectfully requests that the documents submitted herein be considered and made of record in this application.

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Pursuant to CFR § 1.97(c)(2), because this Statement is being submitted after the mailing of the first Office Action on the merits, please charge Deposit Account 16-0085, Reference 8654/2222 for the requisite fees.

Date: May 10, 2005

~~Respectfully submitted,~~



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USPTO Form 1449 U.S. Department of Commerce
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INFORMATION DISCLOSURE STATEMENT

Attorney Docket No.

8654/2222

Serial No.

10/790,943

Applicant(s): Wilson & Siim

Filing Date: March 2, 2004

Group: 1614

U.S. PATENT DOCUMENTS

Examiner Initial		Patent No.	Date	Name	Class	Subclass	Filing Date (if appropriate)
	1.	2001/0027210 A1	Oct. 4, 2001	Wilson	514	455	
	2.	5,620,875	Apr. 15, 1997	Hoffman, et al.	435	123	
	3.	5,281,620	Jan. 25, 1994	Denny, et al.	514	455	
	4.	5,910,505	Jun. 8, 1999	Fleisch, et al.	514	381	
	5.	5,817,684	Oct. 6, 1998	Fleisch, et al.	514	381	

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Publication Date	Country	Class	Subclass	Translation	
							YES	NO
	6.	2001247459	11 Sept. 2001	Japan	A61K	31/352		
	7.	EP 0743 064 A1	20 Nov. 1996	Europe	A61K	31/19		
	8.	WO 00/48591	24 August 2000	PCT	A61K	31/198		
	9.	WO 96/36347	21 Nov. 1996	PCT	A61K	38/00		
	10.	EP 0 584 001 A1	23 Feb. 1994	Europe	A61K	31/335		
	11.	EP 0 584 001 B1	14 May 1997	Europe	A61K	31/335		
	12.	WO 95/09621	13 April 1995	PCT	A61K	31/195		
	13.	WO 97/34482	25 Sept. 1997	PCT	A01N	43/00		
	14.	WO 98/42334	1 Oct. 1998	PCT	A61K	31/41		
	15.	WO 98/25615	18 June 1998	PCT	A61K	31/495		
	16.	WO 98/25616	18 June 1998	PCT	A61K	31/495		
	17.	WO 98/42345	1 Oct. 1998	PCT	A61K	31/52		
	18.	WO 01/34198 A2	17 May 2001	PCT	A61K	41/00		

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

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	19.	WO 01/34197 A2	17 May 2001	PCT	A61K	41/00		
	20.	WO 01/34137 A2	17 May 2001	PCT	A61K	31/00		
	21.	WO 98/25600	18 June 1998	PCT	A61K	31/19		
	22.	WO 98/42335	1 Oct. 1998	PCT	A61K	31/41		
	23.	WO 98/42332	1 Oct. 1998	PCT	A61K	31/35		
	24.	WO 98/42336	1 Oct. 1998	PCT	A61K	31/41		
	25.	WO 98/42337	1 Oct. 1998	PCT	A61K	31/41		
	26.	WO 98/42346	1 Oct. 1998	PCT	A61K	31/52		
	27.	WO 98/42650	1 Oct. 1998	PCT	C07C	63/04		
	28.	WO 00/10600	2 March 2000	PCT	A61K	39/00		
	29.	WO 00/10600 A3	2 March 2000	PCT	A61K	39/00		
	30.	WO 00/16798	30 March 2000	PCT	A61K	38/28		
J	31.	WO 01/34135 A2	17 may 2001	PCT	A61K	31/00	2	

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)		
	32.	Kanwar, et al.; "Taking lessons form dendritic cells: Multiple xenogeneic ligands for leukocyte integrins have the potential to stimulate anti-tumor immunity"; <u>Gene Therapy</u> ; 1999; 6: 1835-1844.
	33.	Kanwar, et al.; "Vascular Attack by 5,6-Dimethylxanthenone-4-acetic Acid Combined with B7.1 (CD80)-mediated Immunotherapy Overcomes Immune Resistance and Leads to the Eradication of Large Tumors and Multiple Tumor Foci ¹ "; <u>Cancer Res.</u> ; 2001; 61: 1948-1956.

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	34.	Hornung, et al.; "Augmentation of Natural Killer Activity, Induction of IFN and Development Tumor Immunity During the Successful Treatment of Established Murine Renal Cancer Using Flavone Acetic Acid and IL-2 ^{1,2} "; <u>The Journal of Immunology</u> ; 1988; 141(10): 3671-3679.					
	35.	Thomsen, et al.; "Nitric Oxide Production in Endotoxin-Resistant C ₃ H/HeJ Mice Stimulated with Flavone-8-acetic Acid and Xanthenone-4-Acetic Acid Analogues"; <u>Biochem. Pharmacol.</u> ; 1992; 43(11): 2401-2406.					
	36.	Lash, et al.; "Enhancement of the anti-tumour effects of the antivasular agent 5,6-dimethylxanthenone-4-acetic acid (DMXAA) by combination with 5-hydroxytryptamine and bioreductive drugs"; <u>Br. J. Cancer</u> ; 1998; 78(4): 439-445.					
	37.	Chaplin, et al.; "Antivasular approaches to solid tumor therapy: evaluation of tubulin binding agents"; <u>Proc. Annu. Am. Assoc. Cancer Res.</u> ; 1996; 37: A3009.					
	38.	Pruijn, et al.; "Mechanisms of enhancement of the antitumour activity of melphalan by the tumour-blood-flow inhibitor 5,6-dimethylxanthenone-4-acetic acid"; <u>Cancer Chemother. Pharmacol.</u> ; 1997; 39(6): 541-546.					
	39.	Vincent, et al.; "Chemotherapy with DMXAA (5,6-dimethylxanthenone-4-acetic acid) in combination with CI-1010 (1H-imidazole-1-ethanol, α -[[(2-bromoethyl)amino]methyl]-2-nitro-, mono-hydrobromide (R isomer)) against advanced stage murine colon carcinoma 26"; <u>Oncol. Rep.</u> ; 1997; 4(1): 143-147.					
	40.	Pedley, et al.; "Enhancement of Antibody-directed Enzyme Prodrug Therapy in Colorectal Xenografts by an Antivasular Agent ¹ "; <u>Cancer Res.</u> ; 1999; 3998-4003.					
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							YES NO
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41.	Cliffe, et al.; "Combining Bioreduction Drugs (SR 4233 or SN 23862) with the Vasoactive Agents Flavone Acetic Acid or 5,6-dimethylxanthene Acetic Acid"; <u>Int. J. Radiation Oncology Biol. Phys.</u> ; (1994); 29(2): 373-377.						
42.	Phillips, R.M.; "Inhibition of DT-diaphorase (NAD(P)H:Quinone Oxidoreductase, EC 1.6.99.2) by 5,6-Dimethylxanthene-4-acetic Acid (DMXAA) and Flavone-8-acetic Acid (FAA): Implications for Bioreductive Drug Development"; <u>Biochem. Pharmacol.</u> ; 1999; 58: 303-310.						
43.	Ching, et al.; "Effect of thalidomide on tumour necrosis factor production and anti-tumour activity induced by 5,6-dimethylxanthene-4-acetic acid"; 1995; <u>Br. J. Cancer</u> ; 72: 339-343.						
44.	Browne, et al.; "Suppression of Serum Tumour Necrosis Factor - α by Thalidomide does not Lead to Reversal of Tumour Vascular Collapse and Anti-Tumour Activity of 5,6-Dimethylxanthene-4-Acetic Acid"; 1998; <u>Anticancer Research</u> ; 18: 4409-4414.						
45.	Ching, et al.; "Interaction of thalidomide, phthalimide analogues of thalidomide and pentoxifylline with the anti-tumour agent 5,6-dimethylxanthene-4-acetic acid: concomitant reduction of serum tumour necrosis factor-alpha and enhancement of anti-tumour activity"; 1998; <u>Br. J. of Cancer</u> ; 78(3): 336-343.						
46.	Kestell, et al.; "Modulation of the pharmacokinetics of the antitumour agent 5,6-dimethylxanthene-4-acetic acid (DMXAA) in mice by thalidomide"; 2000; <u>Cancer Chemother Pharmacol.</u> ; 46: 135-141.						
47.	Cao, et al.; "Thalidomide increases both intra-tumoural tumour necrosis factor- α production and anti-tumour activity in response to 5,6-dimethylxanthene-4-acetic acid"; 1999; <u>Br. J. of Cancer</u> ; 80: 716-723.						
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	48.	Baguley, et al.; "Serotonin involvement in the antitumour and host effects of flavone-8-acetic acid and 5,6-dimethylxanthenone-4-acetic acid"; 1993; <u>Cancer Chemother Pharmacol.</u> ; 33: 77-81.					
	49.	Zwi, et al.; "Correlation Between Immune and Vascular Activities of Xanthenone Acetic Acid Antitumor Agents"; 1994; <u>Oncology Research</u> ; 6(2): 79-85.					
	50.	Zhao, et al.; "Effects of the serotonin receptor antagonist cyproheptadine on the activity and pharmacokinetics of 5,6-dimethylxanthenone-4-acetic acid (DMXAA)"; 2001; <u>Cancer Chemother Pharmacol.</u> ; 47: 491-497.					
	51.	Futami, et al.; "Cytokine Induction and Therapeutic Synergy with Interleukin-2 Against Murine Renal and Colon Cancers by Xanthenone-4-Acetic Acid Derivatives"; 1992; <u>Journal of Immunotherapy</u> ; 12: 247-255.					
	50.	Ching, et al.; "Interaction between endotoxin and the antitumour agent 5,6-dimethylxanthenone-4-acetic acid in the induction of tumour necrosis factor and haemorrhagic necrosis of colon 38 tumours"; 1994; <u>Cancer Chemother Pharmacol.</u> ; 35: 153-160.					
	53.	Ching, et al.; "Induction of Intratumoral Tumor Necrosis Factor (TNF) Synthesis and Hemorrhagic Necrosis by 5,6-Dimethylxanthenone-4-Acetic Acid (DMXAA) IN tnf Knockout Mice ¹ "; 1999; <u>Cancer Research</u> ; 59: 3304-3307.					
	54.	Thomsen, et al.; "Tumor-dependent Increased Plasma Nitrate Concentrations as an Indication of the Antitumor Effect of Flavone-8-acetic Acid and Analogues in Mice ¹ "; 1991; <u>Cancer Research</u> ; 51: 77-81.					
	55.	Baguley, et al.; "Evidence that the 5-hydroxytryptamine antagonist, cyproheptadine, modulates nitric oxide production in mice in response to flavone acetic acid, vinblastine and other agents"; 1992; <u>Biology of Nitric Oxide Part2, Enzymology, Biochemistry and Immunology</u> ; 222-224.					
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56.	Fujii, et al.; "Vaccination with B-1+ tumor and anti-adhesion therapy with RGD pseudo-peptide (FC-336) efficiently induce anti-metastatic effect"; 1998; <u>Clin. Exp. Metastasis</u> ; 16: 141-148.						
57.	Zitvogel, et al.; "Interleukin-12 and B7.1 co-stimulation cooperate in the induction of effective antitumor immunity and therapy of established tumors"; 1996; <u>Eur. J. Immunol.</u> ; 26: 1335-1341.						
58.	Lissoni, et al.; "Neuroimmunotherapy of Advanced Solid Neoplasms with Single Evening Subcutaneous Injection of Low-dose Interleukin-2 and Melatonin: Preliminary Results"; 1993; <u>Eur. J. Cancer</u> ; 29A(2): 185-189.						
59.	Nawrocki & Mackiewicz; "Genetically modified tumour vaccines – where we are today"; 1999; <u>Cancer Treatment Reviews</u> 25: 29-46.						
60.	Thrash-Bingham & Tartof; "aHIF: a Natural Antisense Transcript Overexpressed in Human Renal Cancer and During Hypoxia"; 1999; <u>Journal of the National Cancer Institute</u> ; 91(2): 143-151.						
61.	Rustin, G; "Vascular Targeting in the Clinic"; Abstract; ICTR 2000: 1 st Int'l Conference on Translational Research A.						
62.	Zhou, et al.; "A difference between the rat and mouse in the pharmacokinetic interaction of 5,6-dimethylxanthenone-4-acetic acid with thalidomide"; 2001; <u>Cancer Chemother Pharmacol.</u> ; 47: 541-544.						
63.	Zhou, et al.; "Determination of unbound concentration of the novel anti-tumour agent 5,6-dimethylxanthenone-4-acetic acid in human plasma by ultrafiltration followed by high-performance liquid chromatography with fluorimetric detection"; 2001; <u>J. of Chromatography B</u> ; 757: 359-363.						
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	64.	Zhou, et al.; "Determination of the covalent adducts of the novel anti-cancer agent 5,6-dimethylxanthenone-4-acetic acid in biological samples by high-performance liquid chromatography"; 2001; <u>J. of Chromatography B</u> ; 757: 343-348.					
	65.	Zhou, et al.; "Reversible binding of the novel anti-tumour agent 5,6-dimethylxanthenone-4-acetic acid to plasma proteins and its distribution into blood cells in various species"; 2001; <u>J. of Pharmacy and Pharmacology</u> ; 53: 463-471.					
	66.	Zhou, et al.; "In vitro and in vivo kinetic interactions of the antitumour agent 5,6-dimethylxanthenone-4-acetic acid with thalidomide and diclofenac"; 2001; <u>Cancer Chemother Pharmacol.</u> ; 47: 319-326.					
	67.	Cao, et al.; "Interferon-inducible Protein 10 Induction and Inhibition of Angiogenesis in Vivo by the Antitumor Agent 5,6-Dimethylxanthenone-4-acetic Acid (DMXAA) ¹ "; 2001; <u>Cancer Research</u> ; 61: 1517-1521.					
	68.	Murata, et al.; "Comparative effects of combretastatin A-4 disodium phosphate and 5,6-dimethylxanthenone-4-acetic acid on blood perfusion in a murine tumour and normal tissues"; 2001; <u>Int. J. Radiat. Biol.</u> ; 77(2): 195-204.					
	69.	Zhou, et al.; "Identification of the Human Liver Cytochrome P450 Isoenzyme Responsible for the 6-Methylhydroxylation of the Novel Anticancer Drug 5,6-Dimethylxanthenone-4-Acetic Acid"; 2000; <u>Drug Metabolism and Disposition</u> ; 28: 1449-1456.					
	70.	Siim, et al.; "Scintigraphic Imaging of the Hypoxia Marker ^{99m} Tc-labeled 2,2'-(1,4-Diaminobutane)bis(2-methyl-3-butanone) Dioxime (^{99m} Tc-labeled HL-91; Prognox): Noninvasive Detection of Tumor Response to the Antivascular Agent 5,6-Dimethylxanthenone-4-acetic Acid ¹ "; 2000; <u>Cancer Research</u> ; 60: 4582-4588.					
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	71.	Aitken, et al.; "Synthesis and Antitumour Activity of New Derivatives of Flavone-8-acetic Acid (FAA). Prt 4 ¹ : Variation of the Basic Structure; 2000; <u>Arch. Pharm.</u> ; 333(6): 181-188.					
	72.	Zhou; "Determination of two major metabolites of the novel anti-tumour agent 5,6-dimethylxanthenone-4-acetic acid in hepatic microsomal incubations by high-performance liquid chromatography with fluorescence detection"; 1999; <u>J. of Chromatography B</u> ; 734: 129-136.					
	73.	Ching, et al.; "Induction of STAT and NFκB Activation by the Antitumor Agents 5,6-Dimethylxanthenone-4-acetic Acid and Flavone Acetic Acid in a Murine Macrophage Cell Line"; 1999; <u>Biochemical Pharmacology</u> ; 58: 1173-1181.					
	74.	Kestell, et al.; "Plasma disposition, metabolism and excretion of the experimental antitumour agent 5,6-dimethylxanthenone-4-acetic acid in the mouse, rat and rabbit"; 1999; <u>Cancer Chemother Pharmacol</u> ; 43: 323-330.					
	75.	Joseph, et al.; "Stimulation of Tumors to Synthesize Tumor Necrosis Factor-α in Situ Using 5,6-Dimethylxanthenone-4-acetic Acid: A Novel Approach to Cancer Therapy ¹ "; 1999; <u>Cancer Research</u> ; 59: 633-638.					
	76.	Wilson, et al.; "Enhancement of Tumor Radiation Response by the Antivascular Agent 5,6-Dimethylxanthenone-4-acetic Acid"; 1998; <u>Int. J. Radiation Oncology Biol. Phys.</u> ; 42(4): 905-908.					
	77.	Zaks-Zilberman, et al.; "Induction of Adrenomedullin mRNA and Protein by Lipopolysaccharide and Paclitaxel (Taxol) in Murine Macrophages"; 1998; <u>Infection and Immunity</u> ; 66(10): 4669-4675.					
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78.		Pang, et al.; "Antitumour Activity of the Novel Immune Modulator 5,6-Dimethylxanthenone-4-acetic Acid (DMXAA) in Mice Lacking the Interferon-gamma Receptor"; 1998; <u>European J. of Cancer</u> ; 34(8): 1282-1289.
79.		Baguley, et al.; "Immunomodulatory Actions of Xanthenone Anticancer Agents"; 1997; <u>BioDrugs</u> ; 8(2): 119-127.
80.		Siim, et al.; "Nitro Reduction as an Electronic Switch for Bioreductive Drug Activation"; 1997; <u>Oncology Research</u> ; 9: 357-369.
81.		Baguley, et al.; "Increased Plasma Serotonin Following Treatment with Flavone-8-Acetic Acid, 5,6-Dimethylxanthenone-4-Acetic Acid, Vinblastine, and Colchicine: Relation to Fascular Effects"; 1997; <u>Oncology Research</u> ; 9: 55-60.
82.		Moilanen, et al.; "Persistent induction of nitric oxide synthase in tumours from mice treated with the anti-tumour agent 5,6-dimethylxanthenone-4-acetic acid"; 1998; <u>British J. of Cancer</u> ; 77(3): 426-433.
83.		Philpott, et al.; "Production of tumour necrosis factor- α by cultured human peripheral blood leucocytes in response to the anti-tumour agent 5,6-dimethylxanthenone-4-acetic acid"; 1997; <u>British J. of Cancer</u> ; 76(12): 1586-1591.
84.		Everett, et al.; "High-performance ion chromatography applied to free-radical mechanisms in drug design. The problem of ion analysis at high ionic strengths ¹ "; 1997; <u>J. of Chromatography A</u> ; 770: 273-279.
85.		Patel, et al.; "The Effect of 5,6-Dimethylxanthenone-4-acetic acid on Tumour Necrosis Factor Production by Human Immune Cells"; 1997; <u>Anticancer Research</u> ; 17: 141-150.

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	86.	Miners, et al.; "Preclinical Prediction of Factors Influencing the Elimination of 5,6-Dimethylxanthenone-4-acetic Acid, a New Anticancer Drug ¹ " 1997; <u>Cancer Research</u> ; 57: 284-289.					
	87.	Watts, et al.; "Changes in coagulation and permeability properties of human endothelial cells in vitro induced by TNF- α pr 5.6 MeXAA" 1996; <u>British J. of Cancer</u> ; 74(27): S164-S167.					
	88.	Wilson, et al.; "Tertiary amine N-oxides as bioreductive drugs: DACA N-oxide, nitracrine N-oxide and AQ4N"; 1996; <u>British J. of Cancer</u> ; 74(27): S43-S47.					
	89.	Pedley, et al.; "Ablation of Colorectal Xenografts with Combined Radioimmunotherapy and Tumor Blood Flow-modifying Agents ¹ ; 1996; <u>Cancer Research</u> ; 56: 3293-3300.					
	90.	Wilson & Pruijn; "Hypoxia-Activated Prodrugs as Antitumour Agents: Strategies for Maximizing Tumour Cell Killing"; 1995; <u>Clinical and Experimental Pharmacology and Physiology</u> ; 22: 881-885.					
	91.	Philpott, et al.; "Induction of tumour necrosis factor- α by single and repeated doses of the antitumour agent 5,6-dimethylxanthenone-4-acetic acid"; 1995; <u>Cancer Chemother Pharmacol</u> ; 36: 143-148.					
	92.	Laws, et al.; "Preclinical in vitro and in vivo activity of 5,6-dimethylxanthenone-4-acetic acid"; 1995; <u>British J. of Cancer</u> ; 71: 1204-1209.					
	93.	Webster, et al.; "Metabolism and Elimination of 5,6-Dimethylxanthenone-4-acetic acid in the Isolated Perfused Rat Liver"; 1995; <u>Drug Metab. Dispos. A Publication of the Am. Soc. for Pharm. and Exper. Therapeutics</u> ; 23(3): 363-368.					
	94.	Perera, et al.; "Activation of LPS-Inducible Genes by he Antitumor Agent 5,6-Dimethylxanthenone-4-Acetic Acid in Primary Murine Macrophages"; 1994; <u>J. Immunol</u> ; 153(10): 4684-4693.					
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	95.	Zwi, et al.; "The Morphological Effects of the Anti-Tumor Agents Flavone Acetic Acid and 5,6-Dimethylxanthene Acetic Acid on the Colon 38 Mouse Tumor"; 1994; <u>Pathology</u> ; 26: 161-169.					
	96.	Kestell, et al.; "Disposition of the novel antitumour agent xanthene-4-acetic acid in the mouse: identification of metabolites and routes of elimination"; 1994; <u>Xenobiotica</u> ; 24(7): 635-647.					
	97.	Pedley, et al.; "Enhancement of Radioimmunotherapy by Drugs Modifying Tumour Blood Flow in a Colonic Xenograft Model"; 1994; <u>Int. J. Cancer</u> ; 57: 830-835.					
	98.	Baguley, et al.; "Serotonin involvement in the antitumour and host effects of flavone-8-acetic acid and 5,6-dimethylxanthene-4-acetic acid"; 1993; <u>Cancer Chemother Pharmacol</u> ; 33: 77-81.					
	99.	Everett, et al.; "Decarboxylation of the antitumour drugs flavone-8-acetic acid and xanthene-4-acetic acid by nitrogen dioxide"; 1994; <u>Anti-Cancer Drug Design</u> ; 9: 68-72.					
	100.	Ching, et al.; "Effect of Tumour Growth on the Macrophage Response to the Antitumour Agent 5,6-Dimethylxanthene-4-acetic Acid"; 1993; <u>Anticancer Research</u> ; 13: 2069-2076.					
	101.	Ching, et al.; "Induction of Tumour Necrosis Factor- α Messenger RNA in Human and Murine Cells by the Flavone Acetic Acid Analogue 5,6-Dimethylxanthene-4-acetic Acid"; 1994; <u>Cancer Research</u> ; 54: 870-872.					
	102.	Thomsen, et al.; "Nitric oxide: its production in host-cell-infiltrated EMT6 spheroids and its role in tumour cell killing by flavone-8-acetic acid and 5,6-dimethylxanthene-4-acetic acid"; 1992; <u>Cancer Chemother Pharmacol</u> ; 31: 151-155.					
	103.	Veszelyovszky, et al.; "Flavone Acetic Acid and 5,6-Dimethylxanthene-4-acetic Acid: Relationship between Plasma Nitrate Elevation and the Induction of Tumour Necrosis"; 1993; <u>Eur. J. Cancer</u> ; 29A(3): 404-408.					
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	104.	Gamage, et al.; "Structure-activity relationships for substituted 9-oxo-9, 10-dihydroacridine-4-acetic acids: analogues of the colon tumour active agent xanthenone-4-acetic acid"; 1992; <u>Anti-Cancer Drug Design</u> ; 7: 403-414.					
	105.	Ching, et al.; "Antitumour responses to flavone-8-acetic acid and 5,6-dimethylxanthenone-4-acetic acid in immune deficient mice"; 1992; <u>Br. J. Cancer</u> ; 66: 128-130.					
	106.	Ching, et al., "Stimulation of macrophage tumouricidal activity by 5,6-dimethyl-xanthenone-4-acetic acid, a potent analogue of the antitumour agent flavone-8-acetic acid"; 1992; <u>Biochemical Pharmacology</u> ; 44(1): 192-195.					
	107.	Thomsen, et al.; "Nitric Oxide Production in Endotoxin-Resistant C3H/HeJ Mice Stimulated with Flavone-8-Acetic Acid and Xanthenone-4-Acetic Acid Analogues"; 1992; <u>Biochemical Pharmacology</u> ; 43(11): 2401-2406.					
	108.	Thomsen, et al.; "Modulation of superoxide production form murine macrophages by the antitumour agent flavone acetic acid and xanthenone acetic acid analogues"; 1992; <u>Biochemical Pharmacology</u> ; 43(2): 386-389.					
	109.	Ching, et al.; "In vitro Methods for Screening Agents with an Indirect Mechanism of Antitumour Activity: Xanthenone Analogues of Flavone Acetic Acid"; 1991; <u>Eur. J. Cancer</u> ; 27(12): 1684-1689.					
	110.	Ching, et al.; "Haematological effects in mice of the antitumour agents xanthenone-4-acetic acid, 5,6-methyl-xanthenone-4-acetic acid and flavone acetic acid"; 1991; <u>Cancer Chemother Pharmacol</u> ; 28: 414-419.					
	111.	McKeage, et al.; "Plasma pharmacokinetics of the antitumour agents 5,6-dimethylxanthenone-4-acetic acid, xanthenone-4-acetic acid and flavone-8-acetic acid in mice"; 1991; <u>Cancer Chemother Pharmacol</u> ; 28: 409-413.					
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	112.	Rewcastle, et al.; "Potential Antitumor Agents. 63. Structure-Activity Relationships for Side-Chain Analogues of the Colon 38 Active Agent 9-Oxo-9H-xanthene-4-acetic Acid"; 1991; <u>J. Med. Chem.</u> ; 34: 2864-2870.					
	113.	Zwi, et al.; "Necrosis in non-tumour tissues caused by flavone acetic acid and 5,6-dimethyl xanthenone acetic acid"; 1990; <u>Br. J. Cancer</u> ; 62: 932-934.					
	114.	Ching, et al.; "Induction of Natural Killer Activity by Xanthenone Analogues of Flavone Acetic Acid: Relation with Antitumour Activity"; 1991; <u>Eur. J. Cancer</u> ; 27(1): 79-83.					
	115.	Kestell, et al.; "Determination of xanthenone-4-acetic acid in mouse plasma by high-performance liquid chromatography"; 1991; <u>J. of Chromatography</u> ; 564: 315-321.					
	116.	Thomsen, et al.; "Evidence for the Production of Nitric Oxide by Activated Macrophages Treated with the Antitumor Agents Flavone-8-acetic Acid and Xanthenone-4-acetic Acid"; 1990; <u>Cancer Research</u> ; 50: 6966-6970.					
	117.	Rewcastle, et al.; "Synthesis and Development of two new Classes of Anticancer Drugs: the Tricyclic Carboxamides and the Xanthenoneacetic Acids"; 1989; <u>Chem. N.Z.</u> ; 54(6): 145-150.					
	118.	Rewcastle, et al.; "Light-Induced Breakdown of Flavone Acetic Acid and Xanthenone Analogues in Solution ¹ "; 1990; <u>J. Natl. Cancer Inst.</u> ; 82(6): 528-529.					
	119.	Atwell, et al.; "Synthesis and anti-tumour activity of topologically-related analogues of flavoneacetic acid"; 1989; <u>Anti-Cancer Drug Design</u> ; 4: 161-169.					
	120.	Van der Auwera, et al.; "Conformational Features of Four Model Tripeptides having Piv-Pro-MeXaa-Nme ₂ Sequences"; 1989; <u>Bull. Soc. Chim. Belg.</u> ; 97(3): 199-207.					
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	121.	Rewcastle, et al.; "Potential Antitumor Agents. 58. Synthesis and Structure-Activity Relationships of Substituted Xanthenone-4-acetic Acids Active against the Colon 38 Tumor in Vivo"; 1989; <u>J. Med. Chem.</u> ; 32: 793-799.					
	122.	Griffioen, et al.; "Angiogenesis Inhibitors Overcome Tumor Induced Endothelial Cell Anergy"; 1999; <u>Int. J. Cancer</u> ; 80: 315-319.					
	123.	O'Reilly, et al.; "Endostatin: An Endogenous Inhibitor of Angiogenesis and Tumor Growth"; 1997; <u>Cell</u> ; 88: 277-285.					
	124.	Corbett, et al.; "Activity of flavone acetic acid (NSC-347512) against solid tumors of mice"; 1986; <u>Investigational New Drugs</u> ; 4: 207-220.					
	125.	Shoemaker, et al.; "Pleiotropic Resistance and Drug Development"; 1986; <u>Cancer Drug Resistance</u> ; 143-149.					
	126.	Zaharko, et al.; "Therapeutic and Pharmacokinetic Relationships of Flavone Acetic Acid: An Agent with Activity Against Solid Tumors ^{1,2} "; 1986; <u>Cancer Treatment Reports</u> ; 70(12): 1415-1421.					
	127.	Plowman, et al.; "Flavone Acetic Acid: A Novel Agent with Preclinical Antitumor Activity Against Colon Adenocarcinoma 38 in Mice ^{1,2} "; 1986; <u>Cancer Treatment Reports</u> ; 70(5): 631-635.					
	128.	Biddy & Double; "Flavone acetic acid – from laboratory to clinic and back"; 1993; <u>Anti-Cancer Drugs</u> ; 4: 3-17.					
	129.	Ching & Baguley; "The Anti-Tumour and Immune-Modulatory Activites of Flavone Acetic and Xanthone Acetic Acids"; 1990; N.P. Das (ed.), <u>flavonoids in Biology and Medicine III. Proceeding sof the 3rd International Symposium on Flavonoids in Biology and Medicine</u> ; 381-391.					
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	130.	Biddy, et al.; "Reduction of Tumor Blood Flow by Flavone Acetic Acid: A Possible Component of Therapy"; 1989; <u>J. Natl. Cancer Inst.</u> ; 81: 216-220.					
	131.	Zwi, et al.; "Blood Flow Failure as a Major Determinant in the Antitumor Action of Flavone Acetic Acid"; 1989; <u>J. Natl. Cancer Inst.</u> ; 81: 1005-1013.					
	132.	Jameson, et al.; "Phase I Pharmacokinetic and Pharmacodynamic Study of 5,6-Dimethylxanthene-4-Acetic Acid (DMXAA), A Novel Antivascular Agent"; 2000; <u>Proc. Am. Soc. Clin Oncol.</u> ; 19: 182a.					
	133.	Rewcastle, et al.; "Potential Antitumor Agents. 61. Structure-Activity Relationships for In Vivo Colon 38 Activity Among Disubstituted 9-Oxo-9H-xanthene-4-acetic acids"; 1991; <u>Chemtracts: Org. Chem.</u> 4(2): 168-171.					
	134.	Siim, et al.; "Marked potentiation of the antitumour activity of chemotherapeutic drugs by the antivascular agent 5,6-dimethylxanthene-4-acetic acid (DMXAA); 2003; <u>Cancer Chemother Pharmacol</u> ; 51: 43-52.					
	135.	Baguley, et al.; "Potential of DMXAA combination therapy for solid tumors"; 2002; <u>Expert Rev. Anticancer Ther.</u> ; 2(5): 593-603.					
	136.	Zhou, et al.; "Effects of anticancer drugs on the metabolism of the anticancer drug 5,6-dimethylxanthene-4-acetic (DMXAA) by human liver microsomes"; 2001; <u>J. Clin. Pharmacol.</u> ; 52: 129-136.					
	137.	Wouters, et al.; "Hypoxia as a target for combined modality treatments"; 2002; <u>European J. of Cancer</u> ; 38: 240-257.					
	138.	Wilson; "Combination of the Antivascular Agent DMXAA with Radiation and Chemotherapy"; 2000; <u>International Journal of Radiation Oncology, Biology and Physics</u> ; 46(3): 706.					
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	139.	Combretastatin Update 1: in Ohio Phase I Trial, Some Tumors Respond, Patients Experience Vascular Stress"; 1999; <u>Medical Pike Briefs: Headline Index: Clinical Trial Phase I Results.</u>					
	140.	Atwell, et al.; "Potential Antitumor Agents. 60. Relationships between Structure and in Vivo Colon 38 Activity for 5-Substituted 9-Oxoxanthene-4-acetic Acids"; 1990; <u>J. Med. Chem.</u> ; 33: 1375-1379.					
	141.	Rewcastle, et al.; "Potential Antitumor Agents. 62. Structure-Activity Relationships for Tricyclic Compounds Related to the Colon Tumor Active Drug 9-Oxo-9H-xanthene-4-acetic Acid"; 1991; <u>J. Med. Chem.</u> ; 34: 491-496.					
	142.	Baguley, et al.; "Mechanisms of tumour blood flow inhibition by the antitumour drug DMXAA (5,6-dimethylxanthenone-4-acetic acid"; 2000; <u>Proceeding sof the 11th NCI EORTC AACR Symposium</u> ; Published as a supplement to Clinical Cancer Research; Vol. 6.					
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